UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,988	02/05/2004	Snorri S. Thorgeirsson	11613.29USD1	5511

7590 02/12/2007

Attention: Katherine M. Kowalchyk
MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, MN 55402-0903

EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,988	THORGEIRSSON ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 11 December 2006.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-32 is/are pending in the application.

4a) Of the above claim(s) 8-20, 22, 24-32 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-7,21 and 23 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of group II, claims 1-7, 21, 23, SEQ ID NO:8 in the reply filed on 12/11/06 is acknowledged.

The traversal is on the ground(s) that that other BOG polypeptides SEQ ID NO:2 and SEQ ID NO:10 are orthologues of SEQ ID NO:8 and it would not be undue burden to search all the sequences. This is not found persuasive because different BOG polypeptides SEQ ID NO:2 (rat), SEQ ID NO:8 (human) and SEQ ID NO:10 (murine) are structurally different. Moreover, the searches for different sequences are not co-extensive for reasons already of record, and it would be undue experimentation for one to search all the sequences together.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, Group II, claims 1-7, 21, 23, SEQ ID NO:8 are examined in the instant application.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 21, 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 2 is indefinite, because claim 2 is confusing. It is not clear how a full length sequence is also "a fragment" of said sequence.

2. Claim 3 is indenite for reciting Table 1, 5, or 7 in the claim.

MPEP 2173.05(s) teaches that "Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." *Ex parte Fressola*, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted)".

This rejection could be obviated by amending the claim, for example, to delete Table 1, 5 and 7 and to recite SEQ ID NO:8.

3. Claim 21 is indefinite, because claim 21 is dependent on non-elected claim 20.

4. Claims 1-2, 4-7, 21, 23 are indefinite for the use of designation "BOG polypeptide" as the sole means of identifying the claimed polypeptide. The use of laboratory designation only to identify a particular polypeptide renders the claim indefinite because different laboratories may use the same laboratory designations to define completely distinct polypeptides. Amendment of the claims to incorporate for example, a sequence identification number, to include physical and/or functional characteristics of "BOG polypeptide", which unambiguously define "BOG polypeptide", is suggested.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-7, 21, 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses that BOG polypeptide encompasses native BOG, such as naturally-occurring variant or allelic variant of the BOG, and BOG variants having one or more amino acids added or deleted, at the N- or C-terminus of the sequence of Table 1, 5, or 7 (p.10). The specification discloses that the BOG polypeptide has a putative pRb binding region and two casein kinase II phosphorylation regions flanking the pRb binding region (p. 42, and Table 1 on pages 56-58). The specification shows amino acid sequence homology of the pRb binding region and the casein kinase II phosphorylation region between BOG and the viral protein E7, SV40 LT, or Ad5 E1A and the RBP-1 protein (Table 2 on page 58). The specification discloses that the BOG polypeptide binds to the protein encoded by the tumor suppressor gene, retinoblastoma susceptible gene (RB), and displaces the binding of the transcriptional factor E2F-1 to RB (p.45).

The claimed invention is drawn to a genus of BOG polypeptides identified by the presence of a pRB binding domain, and one or two casein kinase II phosphorylation region. However, the relationship between structure and function of members of the genus has not been defined. There are known proteins, such as the viral protein E7, SV40 LT, or Ad5 E1A and the RBP-1 protein, that also have a pRb binding region and a casein kinase II phosphorylation region, but are functionally and structurally different from the claimed BOG polypeptide SEQ ID NO:8 (the instant specification, tables 2-3 on pages 58-59). Further, Phillips et al, 1997, J Gen

Virol, 78 (pt 4): 905-9, teach that besides the pRB binding domain, and the casein kinase II phosphorylation region, the C-terminal dimerization domain and N-terminal domain are also necessary for full E7 function (p.905, second column). Phillips et al teach that although the viral E7 protein transforming and immortalizing activity is mediated in part through the interaction with the pRB protein via the pRb bindind domain, this interaction with pRb protein is not solely responsible for E7 function, and other property of E7 such as interaction with the transcriptional factor TBP (abstract). In other words, a polypeptide comprising only two domains, the pRB binding domain, and the casein kinase II phosphorylation region, as claimed in claim 1, does not define the function of the polypeptide. Moreover, the viral E7 protein, although contains a pRB binding domain, and a casein kinase II phosphorylation region, having at most 38% homology to the rat BOG polypeptide SQ ID NO: 2 (the instant specification, page 59). In view of the above, there is **no correlation between structure and function** of the claimed genus of polypeptides. Applicant has not shown that the presence of a pRB binding domain, and one or two casein kinase II phosphorylation regions alone is sufficient to confer the BOG property, such as displacement of the binding of the transcriptional factor E2F-1 to RB. In the absence of such a relationship, either disclosed in the as filed application or which would have been recognized based upon information readily available to one skilled in the art, the skilled artisan would not know how to make compounds that lack structural definition.

This situation is analogous to that of *Regents of the University of California v Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d

1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that □the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

In this case, the specification does not describe the BOG polypeptide in a manner that satisfies either the standards as shown in the example of Lilly or Enzo. The specification does not provide sufficient structure or common structure, other than SEQ ID NO: 8, to support the broad breath of the claimed genus. Nor is there any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses SEQ ID NO: 8, this does not provide a description of the BOG polypeptide that would satisfy the standard as shown in the example of Enzo.

The specification also fails to describe the BOG polypeptide, by the standards shown in the example in Lilly. The specification describes only SEQ ID NO: 8. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus." To comply with the written description requirement of 35 U.S.C. § 112, first paragraph, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.

The specification does not provide an adequate written description of the BOG polypeptide that is required to practice the claimed invention. Thus, the specification does not meet the 112, first paragraph written description requirement, and one of skill in the art would reasonably conclude that Applicant did not have possession of the claimed BOG polypeptide at the time the invention was made.

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

Claims 1-2, 4-7, 21, 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the BOG polypeptide SEQ ID NO:8, does not reasonably provide enablement for a polypeptide comprising a BOG polypeptide fragment, comprising a PRb binding motif and one or two casein kinase II phosphorylation motif. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

To comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must enable one skilled in the art to make and use the claimed invention without undue experimentation. The claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims. Such an analysis does not need to specifically enumerate (points 1-8) but only needs to have a select few of the factors present discussed in a rejection.

The disclosure in the specification has been set forth above.

The claimed invention is drawn to a genus of BOG polypeptides identified by the presence of a pRB binding domain, and one or two casein kinase II phosphorylation region. However, the relationship between structure and function of members of the genus has not been defined, supra. In the absence of such a relationship, either disclosed in the as filed application or which would have been recognized based upon information readily available to one skilled in the art, the skilled artisan would not know how to make and use compounds that lack structural and functional definition. Further, an assay for finding a product is not equivalent to a positive recitation of how to make such as product.

Therefore, it would be undue experimentation for one of skill in the art to practice the claimed invention.

Claim Rejections - 35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Phillips et al, 1997, J Gen Virol, 78 (pt 4): 905-9.

Claim 1 is drawn to: An isolated polypeptide comprising a BOG polypeptide fragment, said BOG fragment comprising a pRb binding motif and a casein kinase II phosphorylation motif.

Claim 2 is drawn to: The BOG polypeptide fragment of claim 1, wherein said BOG polypeptide fragment is a full length BOG polypeptide.

Claim 3 is drawn to: The BOG polypeptide fragment of claim 1, comprising "an amino acid sequence" as shown in Table 1, 5 or 7 (SEQ ID NO:8).

Claim 4 is drawn to: The BOG polypeptide fragment of claim 1, wherein said casein kinase II phosphorylation motif is located downstream of the pRb binding motif.

Claim 21 is drawn to: A BOG polypeptide fragment produced by the method of claim 20.

Due to the language "an amino acid sequence", claim 3 is reasonably interpreted as a BOG fragment of claim 1, comprising an amino acid sequence as little as two amino acids of SEQ ID NO:8. Further, claim 21 is a product by process, and is treated as the product per se, that is a BOG polypeptide fragment of claim 1.

Phillips et al teach the full length viral E7 protein, which has a pRb binding region and a casein kinase II phosphorylation region, C-terminal to or downstream of the pRb binding region (figure 1 on page 906). Further, the E7 protein has amino acids SS (as evidenced by the instant specification, page 59, line 8), which is the same as the amino acids SS of SEQ ID NO:8 (table 5 on page 60 of the instant specification).

The protein taught by the art seems to be the same as the claimed polypeptide.

Although the reference does not explicitly teach that the protein is a BOG polypeptide, however, the claimed polypeptide appears to be the same as the prior art protein. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 7, 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips et al, 1997, J Gen Virol, 78 (pt 4): 905-9, supra, in view of US 5,188,943 (Reddington et al, filed on 10/09/1990).

Claim 6 is drawn to: The BOG polypeptide fragment of claim 1 joined to a detectable label.

Claim 7 is drawn to: The BOG polypeptide fragment of claim 6, wherein the detectable label includes a radioactive isotope, an enzyme, a chromophore or a mixture thereof.

Claim 23 is drawn to: A chimeric molecule comprising a BOG polypeptide fragment fused to a heterologous amino acid sequence.

The teaching of Phillips et al has been set forth above.

Phillips et al do not teach joining the polypeptide with a detectable label, which could be a radioactive isotope, an enzyme, a chromophore or a mixture thereof. Phillips et al do not teach chimeric molecule comprising a BOG polypeptide fragment fused to a heterologous amino acid sequence.

US 5,188, 943 teaches tagging of an antibody with a tag, such as an enzyme, to measure how much tagged antibody is present (column 4, last paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to tag the polypeptide taught by Phillips et al with a label such as an enzyme, using the method taught by US 5,188, 943 to facilitating detection the polypeptide. It is noted that the enzyme is an amino acid sequence heterologous to the polypeptide taught by Phillips et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SHANON FOLEY can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
January 31, 2007

Shanon H. Foley
SHANON FOLEY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600